

REMARKS

Claims 23 to 36 remain in this application. Claims 1-22 have been cancelled.

Claims 30 and 35 have been amended.

Applicants thank the Examiner for entering the amendments filed on June 25, 2003.

Claim rejections under 35 U.S.C. § 112, second paragraph, indefiniteness

Claims 23-36 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants traverse these rejections. The remarks presented below show that Claims 23-36 particularly point out and distinctly claim the subject matter which the Applicants regard as their invention, as required under 35 U.S.C. § 112, second paragraph. Therefore, the outstanding rejections under 35 U.S.C. § 112, second paragraph should be withdrawn and Claims 23-36 should be found in condition for allowance.

Regarding the term "bacterial polysaccharide fraction" and the preamble of Claim 23

The term "a method for the isolation of polysaccharides" in the preamble of Claim 23 is objected to, on grounds that reciting "a bacterial polysaccharide fraction" in step (a) means polysaccharides have already been isolated. (Office Action, page 2, lines 16-18; underlining in Office Action). There is a suggestion to amend the preamble to recite "[a] method for the isolation of endotoxins from a polysaccharide fraction" on grounds that the "current method would not adequately remove isolate [sic] polysaccharide from whole cell bacteria which is what the current preamble suggests." (Office Action page 3, lines 1-2). Applicants disagree.

According to the MPEP, "[d]efiniteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made." MPEP § 2173.02 With respect to the statement that reciting "a bacterial polysaccharide fraction" in step (a) means polysaccharides have already been isolated, Applicants point out that the specification teaches states that "[t]he invention relates to a method for the isolation of polysaccharides, in

particular for the separation of endotoxins from capsule polysaccharides of gram-negative bacteria.” (Page 1, lines 2-3). One of skill in the pertinent art would understand that the term “bacterial polysaccharide fraction” indicates a heterogeneous preparation from which polysaccharides can be isolated. In light of the content of the application disclosure and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made, it is clear that polysaccharides can be isolated from a bacterial polysaccharide fraction. Therefore, Claim 23 clearly and precisely recites a method for the isolation of polysaccharides from a bacterial polysaccharide fraction.

With respect to the suggestion that the preamble should be amended to recite “[a] method for the isolation of endotoxins from a polysaccharide fraction,” Applicants point out that the specification teaches that “[t]he invention relates to a method for the isolation of polysaccharides, in particular for the separation of endotoxins from capsule polysaccharides of gram-negative bacteria.” (Page 1, lines 2-3) and the preamble of Claim 23 recites “[a] method for the isolation of polysaccharides.” Therefore, Claim 23 apprises one of ordinary skill in the art of its scope and serves the notice function required by 35 U.S.C. § 112, second paragraph (MPEP §2173.02, citing *Solomon v. Kimberly-Clark Corp.*, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000)), and does not need to be amended.

Regarding the limitation “at which endotoxins are precipitated” in Claim 23

Claim 23 is allegedly vague and confusing on grounds that it is unclear what concentration the limitation “at which endotoxins are precipitated” would encompass. It is further argued that there is no support for this limitation because the specification fails to recite “addition of alcohol to a final concentration *at which endotoxins are precipitated and* which is below the concentration at which the polysaccharide precipitates.” (Office Action, page 3, lines 4-7, emphasis as found in Office Action). Applicants traverse this rejection.

“The test for definiteness under 35 U.S.C. 112, second paragraph is whether ‘those skilled in the art would understand what is claimed when the claim is read in light of the specification.’” MPEP § 2173.01, citing *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Further, “[t]here is no requirement that the words in the

claim must match those used in the specification disclosure.” MPEP § 2173.05(e). Here, the specification teaches that addition of alcohol as claimed in step (b) results in precipitation of endotoxins. In particular, the specification teaches the steps of a method for isolation of polysaccharides on page 2 at lines 11-18, and further teaches that “*the reaction, i.e., the precipitation of endotoxin from the polysaccharide solution*, is conventionally carried out from 1 minute up to 1 hour.” (Page 2 at lines 26-27, emphasis added). The specification discloses an embodiment of the method of the invention in which “alcohol is added in step (b) to the solution to a final concentration which is approximately 10% below the concentration at which the polysaccharide precipitates” and further discloses that “the addition of alcohol in step (b) to this final concentration is particularly advantageous as the loss of polysaccharide in the presence of this concentration is small, *and endotoxin nonetheless is efficiently precipitated.*” (Page 4 at lines 13-19). Example 1 provides an example of practicing the embodiment taught on page 4 at lines 13-19, disclosing addition of ethanol to a final concentration which is about 10% below the concentration at which the polysaccharide begins to precipitate (page 7 at lines 23-25), followed by separation of endotoxins by filtration. (Page 8, lines 1-2). Because the Applicants have used terms and phrases that define the claim limitation “at which endotoxins are precipitated” with a reasonable degree of clarity and precision, the rejection under 35 U.S.C. §112, second paragraph, should be withdrawn.

Regarding the deep bed filter limitation in Claims 34 and 35

Claims 34 and 35 are allegedly vague and confusing as to whether the polymer filter is a deep bed filter. Applicants traverse this rejection. “A claim which makes reference to a preceding claim to define a limitation is an acceptable claim construction which should not necessarily be rejected as improper or confusing under 35 U.S.C. 112, second paragraph.” MPEP §2173.05(f). Applicants point out that Claim 34 is dependent on Claim 23, which recites a deep bed filter in step (d). Therefore, Claim 34 is to a method of isolating polysaccharides according to Claim 23, wherein the deep bed filter used in step (d) is a polymer deep bed filter. Claim 35 has been amended to delete the phrase “and/or the deep bed filter” thereby obviating the rejection of Claim 35.

Regarding the deep bed filter limitation in Claims 23-36

Claims 23-36 are allegedly vague and indefinite regarding whether the deep bed filter is charged, on grounds that “[t]he prior art seemed to indicate that a positively charged depth bed filter was required to trap endotoxins.” (Office Action, page 3, lines 5-17) Applicants traverse this rejection. According to the MPEP, if the examiner concludes that a rejection under 35 U.S.C. 112, second paragraph, is appropriate, then “an analysis as to why the phrase(s) used in the claim is ‘vague and indefinite’ should be included in the Office action.” MPEP §2173.02. Here, the Examiner has neither identified the prior art being relied upon for this rejection, nor the disclosure in this unidentified prior art that seemed to indicate that a positively charged depth bed filter was required to trap endotoxins. Likewise, no analysis has been presented to show how these unidentified disclosures are relevant to a consideration of clarity and precision of Claims 23-26. Therefore, this rejection is improper and should be withdrawn.

Claim rejections under 35 U.S.C. § 112, first paragraph, written description

Claim 23 stands rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the term “at which endotoxins are precipitated” is rejected as new matter. Applicants traverse this rejection.

“Mere rephrasing of a passage does not constitute new matter. Accordingly, a rewording of a passage where the same meaning remains intact is permissible” MPEP § 2163.07, citing *In re Anderson*, 176 USPQ 331 (CCPA 1973). Here, the limitation “at which endotoxins are precipitated” in step (b) is not new matter because the specification teaches that addition of alcohol as claimed in step (b) results in precipitation of endotoxins. In particular, the specification teaches the steps of a method for isolation of polysaccharides on page 2 at lines 11-18, and further teaches that “*the reaction, i.e., the precipitation of endotoxin from the polysaccharide solution, is conventionally carried out from 1 minute up to 1 hour.*” (Page 2 at lines 26-27, emphasis added). The specification discloses an embodiment of the method of the

invention in which “alcohol is added in step (b) to the solution to a final concentration which is approximately 10% below the concentration at which the polysaccharide precipitates” and further discloses that “the addition of alcohol in step (b) to this final concentration is particularly advantageous as the loss of polysaccharide in the presence of this concentration is small, *and endotoxin nonetheless is efficiently precipitated.*” (Page 4 at lines 13-19). Because the limitation “at which endotoxins are precipitated” is supported in the original description, the amendment to add this limitation is not new matter and the rejection of Claim 23 under 35 U.S.C. §112, first paragraph, should be withdrawn.

Claim rejections under 35 U.S.C. § 103(a), obviousness

Claims 23 to 36 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gotschlich *et al.* (*J. Exp. Med.* 129:1349 (1969)) or Schneerson *et al.* (*J. Exp. Med.* 152:361 (1980)) in view of Hou *et al.* (*J. Parenteral Science and Technology* 44:204 (1990)) and Lewis (U.S. Patent No. 5,589,591). In particular, Claims 23-36 are rejected on grounds that “[i]t would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use a depth filter (deep bed filter) with a polymer filter to remove the endotoxins from the polysaccharides isolated by Gotschlich *et al.* or Schneerson because both [sic] Hou teaches that the endotoxins are highly toxic and must be removed from pharmaceutical products prior to use.” (Office Action, page 6 at lines 4-8). It is argued that Hou *et al.* provides motivation in choosing a depth filter for removing endotoxin because Hou *et al.* allegedly disclose that the positively charged depth filter is an effective, economical and practical method for endotoxin removal from large volumes. (Office Action page 6, at lines 11-14). Applicants traverse this rejection.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See*, MPEP §§ 2142, 2143.

As shown in the remarks below, the Examiner has not established a *prima facie* case of obviousness. The combination of cited references does not teach all the claim limitations. The cited references provide neither a suggestion or motivation to combine the reference teachings, nor a reasonable expectation of success from such a combination. Because no criterion for a *prima facie* case of obviousness has been satisfied, the rejection of Claims 23-36 under 35 U.S.C. §103(a) is improper and should be withdrawn.

The combination of references do not teach or suggest all the claim limitations

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka* 180 USPQ 580 (CCPA 1974). In the present case, no cited reference or combination of references teaches all the claim limitations. Applicants point out that the Hou *et al.* reference discloses using a positively charged depth bed filter to remove endotoxin from *aqueous solutions and buffers through charge interaction* (emphasis added). (Hou *et al.*, entire article; see especially, Abstract at line 3 and lines 6-8, page 208 right column at lines 7-9, page 207 left column at lines 33-35, page 208 left column at lines 9-12). The suggested combination of Gotschlich *et al.* or Schneerson *et al.* disclosing isolation of polysaccharides (Office Action page 5 at lines 6-14), with Hou *et al.* disclosing the use of a positively charged depth bed filter to remove endotoxin from aqueous solutions and buffers through charge interaction, does not teach the claim limitations of the present invention. That is, the suggested combination of references does not teach claim limitations of mixing a bacterial polysaccharide fraction with a detergent solution, addition of alcohol to a final concentration at which endotoxins are precipitated and which is below the concentration at which the polysaccharide precipitates, mixing the solution, filtering the solution by way of a deep bed filter wherein the endotoxins are separated and remain in the filter, and separation of the polysaccharide from detergent and alcohol. Because this criterion for a *prima facie* case of obviousness has not been satisfied, the rejection of Claims 23-36 under 35 U.S.C. §103(a) is improper and should be withdrawn.

No suggestion or motivation to combine references to make the claimed invention

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 5 USPQ 2d 1596 (Fed. Cir. 1988); *In re Jones*, 21 USPQ2d 1941 (Fed. Cir. 1992). See generally, MPEP §2143, especially §2143.01. As noted above, the combination of Gotschlich *et al.* or Schneerson *et al.* with Hou *et al.*, does not teach the claim limitations of the present invention. Therefore, there is no teaching, suggestion, or motivation to combine the cited references to produce the claimed invention. Because this criterion for a *prima facie* case of obviousness has not been satisfied, the rejection of Claims 23-36 under 35 U.S.C. §103(a) is improper and should be withdrawn.

No reasonable expectation of success

Prima facie obviousness requires a reasonable expectation of success. The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 231 USPQ 375 (Fed. Cir. 1986). As noted above, the combination of Gotschlich *et al.* or Schneerson *et al.* with Hou *et al.*, does not teach the claim limitations of the present invention. Applicants maintain that the cited references, alone or in combination, do not provide any expectation that such a combination would be successful in producing the claimed invention. Because this criterion for a *prima facie* case of obviousness has not been satisfied, the rejection of Claims 23-36 under 35 U.S.C. §103(a) is improper and should be withdrawn.

Regarding concentrations recited in Claims 30-32

According to the Office Action, the concentrations recited in dependent claims 30-32 are allegedly result effective variables (Office Action, page 7 at lines 13-14) and, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures. (Office Action, page 8 at lines 4-6). Applicants disagree.

Applicants point out that the threshold issue is whether the disclosure(s) of the prior art would have enabled one of ordinary skill to practice the claimed invention. As discussed above, the cited prior art does not even disclose the claimed invention, let alone enable one of ordinary skill to practice the claimed invention. Further, a particular parameter must first be recognized as a result-effective variable before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 195 USPQ 6 (CCPA 1977). Because the cited prior art does not disclose or enable the claimed invention, the concentrations recited in Claims 30-32 were not recognized in the art as result-effective variables. Therefore, it would not have been obvious for one of ordinary skill to discover the concentrations recited in Claims 30-32, because discovery of the concentrations recited in Claims 30-32 is not discovery of optimum workable ranges of methods disclosed by the prior art.

Regarding all rejections under 35 U.S.C. § 103(a)

In sum, no *prima facie* case of obviousness has been established. The cited references fail to teach or suggest all the claim limitations of Claims 23-36. The cited references fail to teach or suggest combining or modifying the references to produce the claimed invention. The cited references provide no guidance as to how to combine or modify references to produce the claimed invention, and provide no reasonable expectation of success from combining or modifying the methods in the cited references. Thus, it cannot objectively be stated that the skilled artisan could modify or combine the references in such a way as to produce the claimed methods, let alone that the skilled artisan would be motivated to combine these references or that there would be a reasonable expectation of success. Finally, because the disclosure(s) of the prior art do not teach the claimed invention, the concentrations recited in Claims 30-32 are not result-effective variables. Therefore, rejection of Claims 23-36 under 35 U.S.C. §103(a) is improper and must be withdrawn.

CONCLUSION

For the reasons set forth herein, Applicants maintain that the pending claims clearly and patentably define the invention, and respectfully request that a timely Notice of Allowance of Claims 23-36 be issued in this case.

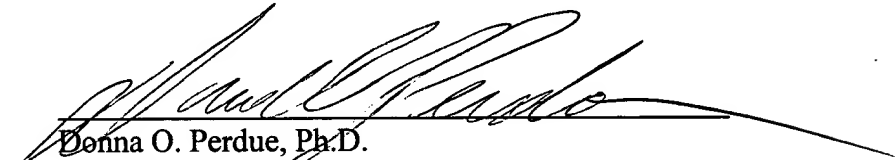
If the Examiner would like to discuss any of the issues raised in this Amendment, Applicant's representative can be reached at (858) 509-4093.

Because this Response is being filed within three months of the mailing date of the Office Action, Applicants believe that no fees for extensions of time are due. If any fees are due, please charge any additional fees, or make any credits, to Deposit Account No. 50-2212.

Respectfully submitted,

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